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REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1-13 and 21-25, the only claims pending and under examination in this application.

Claim 1 has been amended to clarify that what is being detected is of a binding complex of a depurination probe and a target nucleic acid. Claim 21 has been amended to clarify that what is being detected is of a binding complex of a nucleic acid ligand and an analyte. Accordingly, no new matter has been added by way of these amendments and their entry is respectfully requested.

Claim Rejections -35 U.S.C. § 102

Claims 21 and 23-25 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by McGall (US Patent No. 5,843,655).

Claim 21 is directed to a method of detecting the presence of a nucleic acid analyte in a sample. The method includes contacting a nucleic acid array that contains both a set of two or more nucleic acid depurination features, each having a depurination probe, and a nucleic acid ligand that specifically binds to the nucleic acid analyte, with a sample that is suspected of including the analyte under conditions sufficient for binding of the analyte to the nucleic acid ligand on the array to occur. The method further includes detecting the presence of binding complexes of the nucleic acid ligand and the analyte on the surface of the array to detect the presence of the nucleic acid analyte in the sample.

Elements of Claim 21 are detecting a nucleic acid analyte in a sample using a nucleic acid array that contains a depurination probe and detecting the presence of binding complexes on the surface of the array to detect the presence of the nucleic acid analyte in the sample.

The Office asserts that McGall teaches these elements and anticipates the claimed invention. In sustaining this rejection the Office points to Example 8 of

McGall and asserts that "oligonucleotides marked with a 'D' are depurination probes" and that the array containing these depurination probes is treated with a sample suspected of containing a nucleic acid analyte. The Applicants respectfully disagree and contend that the Office is mischaracterizing the cited art.

McGall is directed to determining the extent of depurination of oligonucleotides on a substrate that results from a given testing condition. The method includes the use of a substrate containing oligonucleotide linkers having an active site for coupling of nucleotides. The linkers are resistant to cleavage under alkaline conditions. Labels are attached to the linkers. The substrate is then exposed to a test condition. The test condition is one that is to be evaluated for its causation of depurination. The test condition may, but need not, result in the production of depurinated oligonucleotides. Following the test conditions, the substrate is exposed to alkaline conditions. The purpose for exposing the substrate to alkaline conditions is because depurinated oligonucleotides are prone to backbone cleavage when exposed to alkaline conditions. Any depurinated oligonucleotides produced will be cleaved from the substrate and the remaining labeled probes can be detected so as to determine the extent of the dupurination caused by the test conditions. See column 11, lines 20 to 51.

As can be seen with reference to the above passage, to the extent that McGall discloses determining the amount of depurination it is with respect to synthesizing an oligonucleotide on a substrate, labeling the oligonucleotide, subjecting the substrate to a test condition, and then determining the extent of any resultant depurination that may result because of the test condition. At no point in this process is the substrate contacted with a sample suspected of including an analyte. Hence, there is no binding of an analyte to any of the probes, there is no detecting of a binding complex and there is no detection of the presence of an analyte in a sample. Rather, the synthesized probes are merely labeled and subjected to a test condition, wherein one or more of the labeled probes may be cleaved from the array due to a depurination event caused by the test condition and being exposed to cleavage conditions. To the extent that a detection step is involved

it simply includes a detection of the probes remaining on the substrate subsequent to the performance of the test condition.

In view of the above, the Applicants contend that McGall is deficient in that it does not teach all the elements of the rejected claims, namely contacting a nucleic acid array that contains a nucleic acid depurination feature having a depurination probe with a sample that is suspected of including the analyte and detecting the presence of binding complexes on the surface of the array to detect the presence of the nucleic acid analyte in the sample. Therefore, because McGall does not teach all the elements of the rejected claims it fails to anticipate the claimed invention. Consequently, the Applicants respectfully request that the 35 U.S.C. § 102(b) rejection of Claims 21 and 23-25 be withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 1-13 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over McGall in view of Weng *et al.* (US Patent No. 6,691,042).

Claim 1 is directed to a method of detecting the presence of a depurination reaction product on a surface of an in situ produced nucleic acid array. The method includes contacting an in situ produced nucleic acid array that includes at least one depurination probe feature, having a depurination probe, with a sample having a target nucleic acid that specifically binds to the depurination probe. The method further includes detecting the amount of resultant binding complexes of the depurination probe and target nucleic acid in the depurination probe feature so as to determine the presence of depurination reaction products on the surface.

An element of Claim 1 is detecting the amount of resultant binding complexes of the depurination probe and target nucleic acid in the depurination probe feature to determine the presence of depurination reaction products on the surface.

The Office acknowledges that McGall is deficient in that it fails to teach or suggest the use of a hybridization condition as a test condition for determining

depurination. The Office, therefore, relies upon Weng to remedy the deficiencies of McGall. The Office asserts that it would have been obvious to modify the depurination test conditions as taught by McGall with the hybridization conditions disclosed in Weng.

The Applicants, however, respectfully disagree and contend that a *prima facie* case of obviousness has not been established because the recited combination still fails to teach or suggest all the elements of the rejected claims.

As set forth above, an element of Claim 1 is detecting the amount of resultant binding complexes of depurination probes and target nucleic acids in the depurination probe feature to determine the presence of depurination reaction products on the surface. Even if one were to combine the references in the manner suggested, the resultant method would still be deficient in that it would fail to teach or suggest this element of the rejected claims.

Specifically, the Applicants contend that even if McGall were to be modified so as to employ hybridization as a test condition, the proposed combination would not result in detecting the amount of binding complexes of depurination probes and target nucleic acids in the depurination probe feature. The modification of McGall would not result in this element being present because McGall is not concerned with determining binding complexes, but rather to determining a depurination event. Hence, McGall discloses that subsequent to subjecting the substrate to a test condition, the substrate is exposed to cleavage conditions that result in depurinated oligonucleotides being cleaved from the substrate (see column 9, lines 50-53). The remaining probes (e.g., the probes which have not been depurinated) are then detected and the amount of depurination is determined by the reduction in the surface tag in the region subjected to the test condition (see column 9, lines 62-63).

Thus, even if McGall were to be modified in view of Weng, at no point in time would the modified combination teach or suggest detecting an amount of binding complexes of depurination probes and target nucleic acids in a depurination probe feature. Rather, even if modified McGall would still be directed to detecting the

amount of non-depurinated probes that have not been cleaved from the surface of the substrate. Hence, the use of hybridization as a test condition, disclosed by Weng, does nothing to remedy this deficiency.

In view of the above, the Applicants contend that a *prima facie* case of obviousness has not been established because the recited combination fails to teach or suggest all the elements of the rejected claims, namely detecting the amount of binding complexes of a depurination probe and a target nucleic acid in a depurination probe feature. Consequently, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1-13 be withdrawn.

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CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone John Brady at (408) 553-3584.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10030355-1.

Respectfully submitted,

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